
Article:
Camacho, E, Ntais, D, Coventry, Peter orcid.org/0000-0003-0625-3829 et al. (7 more authors) (2016) Long-term cost-effectiveness of collaborative care (vs usual care) for people with depression and comorbid diabetes or cardiovascular disease : a Markov model informed by the COINCIDE randomised controlled trial. BMJ Open. ISSN 2044-6055

https://doi.org/10.1136/bmjopen-2016- 012514

BMJ Open

Long-term cost-effectiveness of collaborative care (vs usual care) for people with depression and comorbid diabetes or cardiovascular disease: a Markov model informed by the COINCIDE randomised controlled trial

Elizabeth M Camacho,[1] Dionysios Ntais,[1] Peter Coventry,[2] Peter Bower,[3] Karina Lovell,[4] Carolyn Chew-Graham,[5,3] Clare Baguley,[6] Linda Gask,[3] Chris Dickens,[7] Linda M Davies[1]

To cite: Camacho EM, Ntais D, Coventry P, *et al*. Long-term cost-effectiveness of collaborative care (vs usual care) for people with depression and comorbid diabetes or cardiovascular disease: a Markov model informed by the COINCIDE randomised controlled trial. *BMJ Open* 2016;**6**:e012514. doi:10.1136/bmjopen-2016-012514

► Prepublication history and additional material is available. To view please visit the journal (http://dx.doi.org/10.1136/bmjopen-2016-012514).

Received 3 May 2016
Revised 4 July 2016
Accepted 9 August 2016

For numbered affiliations see end of article.

Correspondence to
Dr Elizabeth M Camacho; elizabeth.camacho@manchester.ac.uk

ABSTRACT

Objectives: To evaluate the long-term cost-effectiveness of collaborative care (vs usual care) for treating depression in patients with diabetes and/or coronary heart disease (CHD).

Setting: 36 primary care general practices in North West England.

Participants: 387 participants completed baseline assessment (collaborative care: 191; usual care: 196) and full or partial 4-month follow-up data were captured for 350 (collaborative care: 170; usual care: 180). 62% of participants were male, 14% were non-white. Participants were aged ≥18 years, listed on a Quality and Outcomes Framework register for CHD and/or type 1 or 2 diabetes mellitus, with persistent depressive symptoms. Patients with psychosis or type I/II bipolar disorder, actively suicidal, in receipt of services for substance misuse, or already in receipt of psychological therapy for depression were excluded.

Intervention: Collaborative care consisted of evidence-based low-intensity psychological treatments, delivered over 3 months and case management by a practice nurse and a Psychological Well Being Practitioner.

Outcome measures: As planned, the primary measure of cost-effectiveness was the incremental cost-effectiveness ratio (cost per quality-adjusted life year (QALY)). A Markov model was constructed to extrapolate the trial results from short-term to long-term (24 months).

Results: The mean cost per participant of collaborative care was £317 (95% CI 284 to 350). Over 24 months, it was estimated that collaborative care was associated with greater healthcare usage costs (net cost £674 (95% CI −30 953 to 38 853)) and QALYs (net QALY gain 0.04 (95% CI −0.46 to 0.54)) than usual care, resulting in a cost per QALY gained of £16 123, and a likelihood of being cost-effective of 0.54 (willingness to pay threshold of £20 000).

Conclusions: Collaborative care is a potentially cost-effective long-term treatment for depression in patients with comorbid physical and mental illness. The estimated cost per QALY gained was below the threshold recommended by English decision-makers. Further, long-term primary research is needed to address uncertainty associated with estimates of cost-effectiveness.

Trial registration number: ISRCTN80309252; Post-results.

Strengths and limitations of this study

- COINCIDE was a large randomised controlled trial (RCT) of a pragmatic intervention with good retention rates.
- Bias and confounding were minimised using a variety of methods at all stages from study design and recruitment to data analysis.
- There was a notable proportion of missing data; multiple imputation of missing values was used to minimise bias.
- The conclusions reported about the long-term cost-effectiveness of collaborative care are extrapolated from a short-term (4-month) RCT and therefore subject to uncertainty; structural and parameter uncertainty in the economic model were explored in sensitivity analyses.
- The economic model and sensitivity analyses demonstrated good external validity with findings from meta-analyses (clinical effectiveness) and narrative systematic reviews (cost-effectiveness) and results were not sensitive to alternative modelling assumptions.

INTRODUCTION

Major depression is a common disabling condition estimated to affect 3% of the English general population;[1] the prevalence and burden in individuals with long-term physical conditions (such as diabetes or heart disease) is higher still.[2–6] Factors associated with depression, such as poor self-care, can lead to complications and higher mortality from physical health conditions.[7 8] In time-restricted and performance-managed primary care settings, detecting and diagnosing depression in people with long-term conditions can be especially problematic. Patients and healthcare professionals commonly dismiss depression as an inevitable consequence of long-term conditions and favour strategies that prioritise physical health.[9–12]

Global and English health policy has recognised the importance of improving mental health generally and specifically among those with physical health problems.[13 14] In England, government policy has increasingly promoted increased access to mental healthcare through commissioning and provision of health and social care in the primary care setting. This is supported by the Improving Access to Psychological Therapies (IAPT) initiative. It is important to explore ways in which the IAPT initiative can be capitalised on to improve healthcare and health outcomes for patients. Collaborative care is a complex intervention which may provide a framework for delivering IAPT-based treatments. Collaborative care was developed in the USA and involves the use of a case manager working with primary care professionals, often supervised by a mental health specialist and supported by appropriate care management systems that can enhance interprofessional communication and facilitate proactive and scheduled follow-up of patients.[15–17]

A definitive Cochrane review reported that collaborative care effectively treated depression and anxiety over the short (0–6 months), medium (7–12 months) and long term (13–24 months), compared with usual care.[18] The review defined usual care as one of: no additional intervention; the same additional intervention applied to both study arms (effects potentially cancelled out); or enhanced usual care (a non-collaborative intervention that the collaborative care arm did not receive). Much of the evidence is drawn from the USA, where care is organised, provided and funded differently from the UK. However, the COINCIDE and CADET trials showed that the short-term and medium-term benefits of collaborative care also translate to the English healthcare system.[15 19] There is good evidence (from the USA) that collaborative care is also effective for treating depression in people with coexisting long-term physical health conditions.[20–23]

Evidence that collaborative care is *cost*-effective is more limited, and again mostly from the USA.[24 25] However, an economic evaluation of CADET has recently shown that compared with usual care, collaborative care is cost-effective in the medium term (12 months), from the perspective of the English National Health Service (NHS).[26] Analysis of complete-case data in that trial, estimated that collaborative care offered a mean incremental gain of 0.02 (95% CI −0.02 to 0.06) quality-adjusted life years (QALYs) over 12 months, at a mean incremental cost of £270.72 (95% CI −202.98 to 886.04). This resulted in a cost per QALY of £14 248 and a probability of 0.58 that collaborative care was cost-effective if decision-makers are willing to pay £20 000/QALY gained.

The long-term (>12 months) clinical and cost-effectiveness of collaborative care in the English healthcare system have not been evaluated previously. The long-term effectiveness of collaborative care may be particularly relevant to patients with comorbid physical illnesses if an artefact of collaborative care is an altered trajectory of mental and/or physical health needs or long-term improvements in relationships with healthcare practitioners/self-care.[20 27] A trial of a collaborative care for managing depression in patients with cancer reported a higher cost per QALY gained over 5 years than over 20 years, suggesting it may become better value with an increasing time horizon.[28]

The COINCIDE trial was a robust, pragmatic randomised controlled trial (RCT) of collaborative care versus usual care, delivered in routine primary care in the English NHS to trial participants with a long-term condition (diabetes and/or coronary heart disease (CHD)) and depression.[16] Owing to logistical constraints, COINCIDE participants were only followed for 4 months.[17] CHD and diabetes are lifelong conditions, and depression can be a recurrent, chronic condition. Therefore, it is important to consider the effectiveness of collaborative care in this population over long-term periods. Economic models can be used to extrapolate the cost-effectiveness findings from a short-term RCT to longer time horizons and alternative settings and populations.[29]

This study is important because it makes a robust contribution to economic evidence about estimated costs and benefits of implementing collaborative care in the English healthcare system (NHS England). Existing evidence is limited to studies conducted in the US healthcare system which may not be relevant to the implementation of collaborative care in the NHS. Emerging evidence from a single English complete-case analysis suggests that collaborative care may be cost-effective in this context over 12 months. However, it is still unknown whether these findings are likely to translate to longer time horizons. This analysis uses an economic model to estimate the cost-effectiveness of collaborative care in the context of the NHS at 12, 24 and 36 months. This has not been done previously. Furthermore, this is the first analysis of the cost-effectiveness of collaborative care in the NHS for patients with long-term physical conditions alongside depression (multimorbidity).

Aim: To use an economic model to extrapolate trial-based cost-effectiveness estimates for collaborative care versus usual care over a long-term (24 months) time horizon. The key objectives were to:

- Develop an economic model to represent the key health states and events observed during the COINCIDE trial of collaborative versus usual care;
- Estimate the costs of health and social care in the collaborative care and usual care groups;
- Assess whether there are differences in costs between collaborative care and usual care;
- Estimate the health status and QALYs of patients in the collaborative care and usual care groups;
- Assess whether there are differences in health status and QALYs between collaborative care and usual care;
- Estimate the long-term cost-effectiveness of collaborative care, compared with usual care.

METHODS

Randomised controlled trial

The COINCIDE trial was an integrated clinical and economic study to evaluate the effectiveness and cost-effectiveness of a collaborative care intervention in people with diabetes and/or CHD who had comorbid depression. The evaluation was a cluster RCT of 36 primary care (general) practices in the North West of England, randomised to provide either collaborative care or usual care. Randomisation was by a central service, separated from the investigators, using minimisation based on practice size and deprivation. Three hundred and eighty-seven participants were recruited; 191 at practices randomised to deliver collaborative care and 196 at practices delivering usual care. Sixty-two per cent of participants were male, 14% were of non-white ethnicity. The majority (76%) of participants were from moderately/highly deprived areas (54% from highly deprived areas) and had a mean of 6.2 (SD 3.0) medical conditions in addition to diabetes and/or CHD. Full details of the trial design are reported elsewhere.[16 17] practices were eligible for inclusion if they held and maintained a Quality Outcomes Framework (QOF) register of patients with CHD and diabetes mellitus.[30] Patients aged ≥18 years attending each practice were eligible for inclusion if they were listed on either of these QOF registers and had persistent depressive symptoms (≥10 on Patient Health Questionniare-9 (PHQ-9)).[31]

Participants attending practices in the collaborative care arm were offered a choice of appropriate evidence-based low-intensity psychological treatments, delivered over 3 months through IAPT services. Case management was provided jointly by the practice nurse and a Psychological Well Being Practitioner (PWP; graduate psychologists employed by IAPT to provide high-volume, low-intensity psychological interventions).

Participants attending practices allocated to usual care received standard management from their primary care team. Standard management for depression in adults with physical health conditions can vary but should include the components of the National Institute for Health and Care Excellence (NICE) stepped care model which includes support from general practitioners (GPs), referral for a range of low-intensity to high-intensity psychological interventions and/or antidepressant therapy (dependent on severity of depression, patient preference and prior experience).[32] In line with the pragmatic nature of this evaluation, patients in the usual care group could receive antidepressant treatment and referral for psychological therapy, although this was not delivered by a specially trained COINCIDE PWP.

The primary clinical outcome was the difference between the collaborative and usual care groups in the mean score on the 13 depression-related items of the 90-item symptom checklist (SCL-D13)[33] at the end of a 4-month follow-up period. This was collected at follow-up for 170 participants in the collaborative care group and 180 in the usual care group. Participants in the collaborative care arm had a lower mean SCL-D13 depression score (difference −0.23; 95% CI −0.41 to −0.05; adjusted standardised effect size 0.30) and also reported being better self-managers, rated their care as more patient centred and were more satisfied with their care.[19]

Economic evaluation

Measuring health benefit

The primary measure of health benefit for the analysis was the QALY, estimated from the EuroQol five dimension questionnaire, 5-level version (EQ -5D-5L) and associated utility tariffs.[34 35] The EQ-5D is a validated, generic, preference-based measure of health status, widely used in national health surveys in the UK and clinical trials of mental health interventions. The EQ-5D is currently recommended for by the NICE to estimate health state utility weights for the calculation of QALYs.[36] QALYs are estimated as the average time spent in a health state multiplied by the average utility weight associated with it. Despite being a global measure, a systematic review reported that the EQ-5D demonstrates good construct validity and is sensitive to changes in depression.[37] In COINCIDE, there were significant relationships between baseline utility values and clinical outcome measures (SCL-90, Pearson −0.311, p≤0.001; PHQ-9, Pearson −0.307, p≤0.001; World Health Organisation-Quality of Life instrument (WHO-QOL), Pearson 0.448, p≤0.001; generalised anxiety disorder assessment, 7-item version (GAD-7), Pearson −0.231, p≤0.001; Symptom Disruption Score (SDS), Pearson −0.384, p≤0.001; burden of diseases, Pearson −0.454, p≤0.001).

Measuring costs

Data on the resources used to establish and deliver the intervention were collected from activity logs completed by the PWPs and practice nurses delivering collaborative care. In addition to the main and collaborative sessions, this also included note writing and supervisions attended by the PWPs. The costs of training were also included in the primary analysis. Data on the use of other health and social care services were collected by questionnaire completed by participants at initial (4-month) follow-up. The services included primary and community care, hospital

inpatient and outpatient care, prescribed medications, and patient health-related costs and expenses (travel to healthcare appointments and private medical expenses exceeding £50, eg, reflexology). The costs of resources used were estimated as the product of the resource use and its unit cost. The unit costs of the services used were originally derived from the 2011–2012 Reference Costs database (published by the Department of Health), 2011–2012 unit costs of primary and community health and social care services (published by the Personal and Social Services Research Unit), and the 2011–2012 British National Formulary (BNF) handbook[38–40] (see online supplementary table S1). All costs were inflated to 2014/2015 prices, based on the Hospital and Community Health Services (HCHS) Index.[38]

Participants were also asked about support from family and friends. However, a high level of missing data and inconsistency of reporting meant that it was not possible to estimate reliable costs for this resource.

Missing data

Missing data on costs and EQ-5D domains were imputed using the multiple imputation chained-equation procedure, which is robust against assumptions that data are missing not at random. The multiple imputation procedure included baseline covariates identified as predictors of costs and utilities (EQ-5D pain/discomfort, number of additional conditions, Bayliss burden of disease score, PHQ-9 score, SDS, social or family life, ethnicity, employment, GP practice) in addition to age, sex and baseline SCL-D13 score.

Economic model

Both the primary and sensitivity analyses used the framework of cost-effectiveness and cost-effectiveness acceptability analysis to evaluate the potential for collaborative care to be cost-effective in an NHS primary care setting. The perspective for the evaluation was that of the patient (health benefits) and health and social care services (costs)—an approximation of the societal perspective. The target population for the economic model analyses was people with diabetes and/or CHD with comorbid depression. Data from participants in COINCIDE were used to represent this population. Differences between model parameters estimated from COINCIDE data and results reported from other published evaluations were explored in sensitivity analyses (described below).

The time horizon for the primary analysis was 24 months. An annual discount rate of 3.5% was applied to costs and effects for the period beyond 12 months, as per NICE recommendations for economic evaluations in healthcare.[36] The simulation software was TreeAge Pro plus Healthcare. The primary measure of cost-effectiveness for the model analyses was the incremental cost-effectiveness ratio (ICER), reported as cost per QALY gained from collaborative care. This was calculated as:

$$\text{Costs}_{(\text{collaborative care}-\text{usual care})}/\text{QALYs}_{(\text{collaborative care}-\text{usual care})}$$

Model structure

A simple economic model that combined a decision tree and a Markov cohort model was constructed (figure 1). The initial decision tree structure was based on the care pathways and outcomes observed over 4 months in COINCIDE. Decision trees are simple and transparent, clarifying the options of interest. The distribution of participants in terms of allocation to collaborative/usual care and subsequent depression status (SCL-D13<20 not depressed; SCL-D13≥20 depressed[41]) at the end of the initial follow-up period were described in the model.

A Markov cohort model was constructed for each study arm to extrapolate the findings from COINCIDE over a long-term time horizon. Markov models handle both costs and outcomes intuitively which makes them a powerful tool in economic evaluation.[42] They are particularly useful for modelling chronic conditions with fluctuating severity, such as depression, over time. The 24-month time horizon was split into five cycles of 4 months to reflect the transition between depression states observed during the trial. The health states represented in the model were based on the observed outcomes from COINCIDE: depressed, not depressed, dead. The distribution of participants across the health states at the start of the model was different between the study arms, reflecting the observed proportion of participants in each health state at the end of the initial 4-month follow-up. The health states and possible transitions between them were the same for both models.

Probability of events

The probabilities of following the different pathways through the decision tree or moving between the health states in the Markov model were derived from COINCIDE. The proportion of participants in each health state at the end of the initial follow-up was used to estimate the probability of transitioning between health states for the model. All participants recruited to COINCIDE were identified as depressed; this was based on a PHQ-9 score ≥10. There was a proportion of participants in both study arms who did not have a baseline SCL-D13 score ≥20; the estimated probability of becoming depressed was derived from the outcomes of these participants during the trial. Three participants died before outcome data had been collected at the initial 4-month follow-up, both of whom had SCL-D13 scores ≥20 (ie, classified as depressed in this model). This was applied to the primary analysis as depression-related mortality rate of 0.02 over 4 months. Cardiovascular events were not accounted for in the model as data were not available to explore whether/how the intervention was associated with their likelihood and long-term impact on health status.

Modelling resource use, costs and QALYs

The mean cost and SE of resource use (including direct costs of the collaborative care intervention) and utility weights observed in the trial were used to generate point

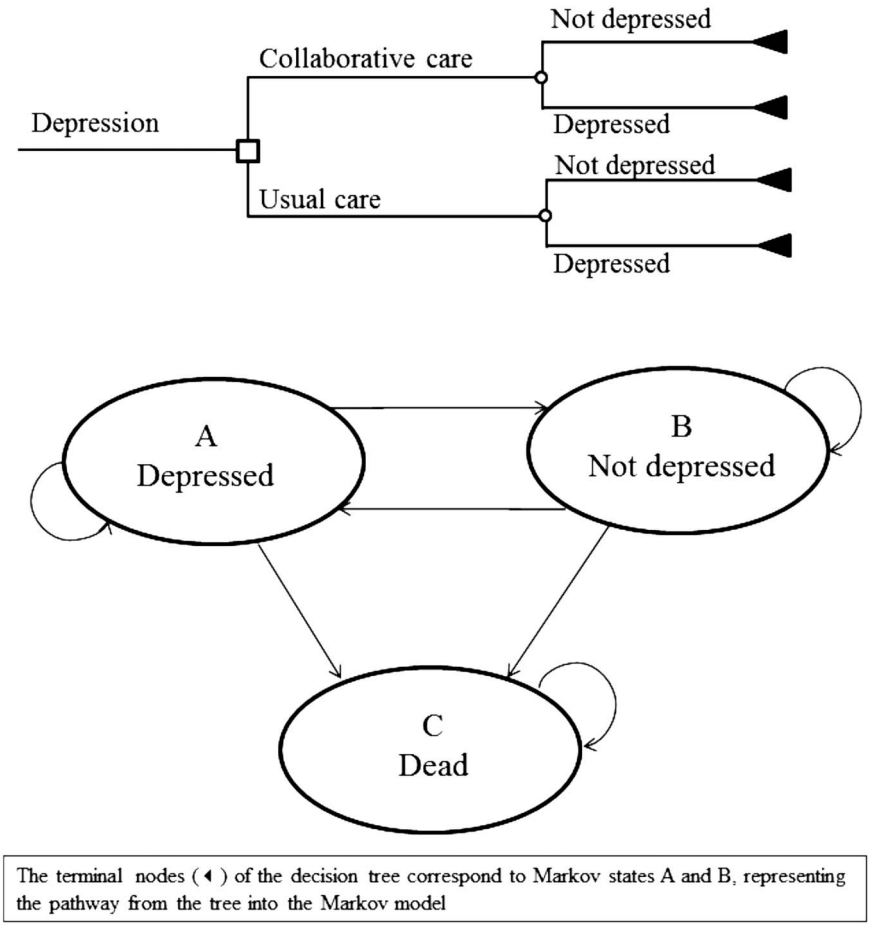

Figure 1 Decision tree and Markov model.

The terminal nodes (◂) of the decision tree correspond to Markov states A and B, representing the pathway from the tree into the Markov model

estimates associated with the different health states in the model. Estimates were produced separately for each intervention group.

The event probability, cost and utility parameters are summarised in table 1. In the primary model, it was assumed that the impact of collaborative care on the utilities associated with each health state and the likelihood of moving between the health states was not sustained beyond the initial 4-month follow-up; utilities and event probabilities were the same in both models. This assumption was explored in one-way sensitivity analyses (described below).

Probabilistic sensitivity analysis

Probabilistic sensitivity analysis (PSA) was used to assess the level of parameter uncertainty (from uncertainty/variance in the data inputs). Each model parameter (event probability, cost or QALY) was assigned a primary value (mean base on data observed from COINCIDE) and a distribution of possible values (see table 1). Monte Carlo simulation was used to estimate mean expected costs and outcomes, and statistical measures of expected variance (SD) around the mean for each of 10 000 iterations drawn from the distributions defined. Each of the 10 000 net outcome estimates were revalued by a willingness to pay threshold (WTPT) of £20 000 (current NICE decision threshold).[36] This was repeated for each of a range of WTPTs. A cost-effectiveness acceptability curve (CEAC) was plotted to show the proportion of bootstrapped simulations where the net benefit of collaborative care was greater than zero for each WTPT.[43–46]

One-way sensitivity analyses

Methodological uncertainty (from the model structure, selection of data inputs or other assumptions) was addressed by one-way sensitivity analysis. For each one-way sensitivity analysis, the parameter of interest was set to a specific value and the PSA and cost-effectiveness acceptability analyses rerun, to assess the robustness of the results to changes in that variable. Parameter values for sensitivity analyses were chosen either as systematic variations around the values in the primary model or from differences between observed data from COINCIDE and CADET and published meta-analyses (clinical effectiveness) and narrative systematic reviews (cost-effectiveness). The parameters tested by one-way sensitivity analysis included time horizon, effectiveness of collaborative care, discount rate for costs and QALYs, mortality rate, and intervention costs.

RESULTS

Within-trial analysis

The probability of being depressed (SCL-D13≥20)[41] at the end of the initial 4-month follow-up was lower for

Table 1 Model parameters for the decision tree and Markov model

	Mean	SE	Distribution
Probabilities*			
Within trial—likelihood of being depressed at follow-up: usual care	0.72	0.030	Triangular 0.72±20%
Within trial—likelihood of being depressed at follow-up: collaborative care	0.57	0.039	Triangular 0.57±20%
Markov transition: not depressed→depressed	0.37	–	Triangular 0.37±20%
Markov transition: remains depressed	0.71	–	Triangular 0.71±20%
Markov transition: depressed→dead	0.02	–	Triangular 0.02±20%
Markov transition: not depressed→dead†	0	–	–
Costs			
Within trial: usual care	1670	203	γ
Within trial: collaborative care	2140	264	γ
Markov state: not depressed	1516	257	γ
Markov state: depressed	1730	219	γ
Markov state: dead	0	–	–
QALYs			
Within trial: usual care	0.169	0.006	β
Within trial: collaborative care	0.185	0.007	β
Markov state: not depressed (usual care)	0.196	0.008	β
Markov state: depressed (usual care)	0.158	0.007	β
Parameters for sensitivity analyses‡			
Markov transition: not depressed→depressed (collaborative care)	0.19	–	Triangular 0.19±20%
Markov transition: remains depressed (collaborative care)	0.56	–	Triangular 0.56±20%
Markov state: not depressed (collaborative care)	0.207	0.005	β
Markov state: depressed (collaborative care)	0.168	0.007	β

*Probabilities not stated in the table are the exhaustive compliment of reported probabilities for each model event.
†Background all-cause mortality assumed to be 0.
‡Primary analysis assumed equivalent probabilities/utilities (usual care) for both trial groups.
QALY, quality-adjusted life year.

participants randomised to collaborative care (0.57, 95% CI 0.50 to 0.65) than usual care (0.72, 95% CI 0.66 to 0.78; p=0.004; imputed data). The mean cost per participant of delivering the collaborative care intervention (including training/supervision/set-up costs) was £317 (£168—when training costs were excluded). The mean (unadjusted) costs of health services used during the trial period was higher for the collaborative care group (£1896, 95% CI 1468 to 2224) than usual care (£1515, 95% CI 1205 to 1826); this included the cost of delivering the intervention and the cost of health services used. Use of health services is summarised by study arm in online supplementary table S1. The mean number of QALYs gained by participants randomised to collaborative care (0.185, 95% CI 0.064 to 0.303) was also higher than usual care (0.169, 95% CI 0.017 to 0.323). Although the mean costs and QALYs were higher for participants randomised to receive collaborative care, compared with usual care, the 95% CIs overlapped substantially, suggesting that these differences were not significant. Within the collaborative care arm, regardless of whether or not participants were depressed at follow-up, the mean QALYs were greater than for the usual care arm (depressed—mean QALYs: collaborative care (0.168); usual care (0.158); non-depressed—mean QALYs: collaborative care (0.207); usual care (0.196)). The ICER for the within-trial model was £29 132/QALY gained from collaborative care with a probability of 0.49 of being cost-effective at a WTPT of £20 000.

Economic model

Table 2 reports the mean costs and QALYs for the intervention groups which were used to calculate the ICER. The estimated cost per QALY gained from collaborative care over a 24-month time horizon (primary analysis) was £16 123. The uncertainty around this estimate is illustrated in figure 2 (represented by the spread of points on the cost-effectiveness plane) and figure 3 (CEAC). The probability that collaborative care is cost-effective (vs usual care) was 0.53 at a WTPT of £20 000 and 0.60 at a WTPT of £60 000 (figure 3). The probability that collaborative care was cost-effective fell below 0.5 at a WTPT of £7000.

Sensitivity analyses

Table 2 presents the results of sensitivity analyses of model assumptions. The results were not sensitive to alternative assumptions about: time horizon, training costs, the benefits of collaborative care over time, mortality rates or discount rates. The ICER changed as expected in response to these assumptions, ranging from £2103 to £22 843 per QALY/gained (over 24 months) with a probability of being cost-effective between 0.52 and 0.65.

Table 2 Cost-effectiveness results—primary and sensitivity analyses

	Mean cost, £ (95% CI)			Mean QALY (95% CI)			Net cost per QALY, £	Probability collaborative care cost-effective (vs usual care)		
	Usual care	Collaborative care	Net cost	Usual care	Collaborative care	Net QALY		WTPT= £15k per QALY	WTPT= £20k per QALY	WTPT= £30k per QALY
Primary										
24-month horizon	9338 (101 to 41 379)	10 012 (125 to 43 131)	674	0.97 (0.39 to 1.77)	1.01 (0.41 to 1.83)	0.04	16 123	0.53	0.54	0.56
Sensitivity										
12-month time horizon	4800 (58 to 19 322)	5359 (75 to 21 596)	560	0.50 (0.22 to 0.87)	0.53 (0.23 to 0.90)	0.03	19 207	0.52	0.53	0.54
36-month time horizon	13 720 (129 to 63 260)	14 507 (160 to 65 497)	787	1.43 (0.54 to 2.68)	1.49 (0.57 to 2.76)	0.05	14 660	0.53	0.56	0.58
Excluding training costs (£131/participant)	9338 (101 to 41 379)	9882 (121 to 42 800)	544	0.97 (0.39 to 1.77)	1.01 (0.41 to 1.83)	0.04	13 005	0.53	0.55	0.57
Waning benefit of CC—33%/cycle	9338 (101 to 41 379)	9959 (123 to 43 517)	620	0.97 (0.39 to 1.77)	1.05 (0.60 to 1.60)	0.08	7854	0.57	0.59	0.60
Waning benefit of CC—25%/cycle	9338 (101 to 41 379)	9941 (122 to 44 344)	602	0.97 (0.39 to 1.77)	1.06 (0.63 to 1.56)	0.09	6673	0.57	0.58	0.60
Waning benefit of CC—10%/cycle	9338 (101 to 41 379)	9891 (119 to 45 312)	553	0.97 (0.39 to 1.77)	1.10 (0.60 to 1.72)	0.13	4399	0.58	0.59	0.61
Maintained benefit of CC	9338 (101 to 41 379)	9858 (114 to 46 215)	520	0.97 (0.39 to 1.77)	1.12 (0.62 to 1.73)	0.15	3468	0.60	0.61	0.62
Growing benefit of CC—25%/cycle	9338 (101 to 41 379)	9788 (99 to 49 796)	450	0.97 (0.39 to 1.77)	1.19 (0.67 to 1.65)	0.21	2103	0.63	0.65	0.66
No deaths during follow-up	9795 (104 to 43 576)	10 278 (127 to 44 497)	483	1.02 (0.40 to 1.87)	1.04 (0.42 to 1.89)	0.02	22 843	0.51	0.52	0.52
Discount rate (costs and QALYs): 0%	9391 (101 to 41 622)	10 066 (125 to 43 368)	675	0.98 (0.39 to 1.78)	1.02 (0.41 to 1.84)	0.04	16 098	0.53	0.54	0.56
Discount rate (costs and QALYs): 5%	9317 (101 to 41 278)	9990 (124 to 43 008)	674	0.97 (0.38 to 1.77)	1.01 (0.41 to 1.82)	0.04	16 133	0.53	0.54	0.56

Mean and net values presented in table have been rounded for clarity—non-rounded values were used to calculate the incremental cost-effectiveness ratios (ICERs).
CC, collaborative care; QALY, quality-adjusted life year; WTPT, willingness to pay threshold.

Subgroup analyses

The model parameters used in subgroup analyses are reported in online supplementary table S2. The parameters were derived from the COINCIDE trial which was not powered for subgroup analyses. As such these parameters are more uncertain than for the whole sample and so results should be interpreted with caution. Online supplementary table S3 presents the results of subgroup analyses on the basis of age at baseline and number of physical conditions reported (in addition to diabetes/CHD). Based on the mean age of the sample (58 years), and the (former) age of retirement for women in England (60 years), two subgroups were defined: under 60 and 60+ years. There was little difference in the likelihood that collaborative care is cost-effective in participants under 60 years old (ICER £16 891; probability cost-effective (£20k/QALY) 0.49) or those older than 60 (ICER £23 358; probability cost-effective (£20k/QALY) 0.49), despite a lower ICER for the under 60 group. This reflects the additional uncertainty around these subgroup estimates. Based on the mean number of long-term conditions reported (other than diabetes or CHD), two subgroups were defined: fewer than 6 conditions and 6+ conditions. Collaborative care may be less likely to be cost-effective in participants with more than six additional conditions (ICER £33 210; probability cost-effective (£20k/QALY) 0.50), compared to those with fewer than six (ICER £9625; probability cost-effective (£20k/QALY) 0.55).

DISCUSSION

Principal findings

The results described here suggest that over a 24-month time horizon, collaborative care, for patients with depression plus comorbid cardiovascular disease and/or diabetes, is potentially cost-effective compared with usual care in the English healthcare system.

Comparison with other studies

The relative risk of depression for usual versus collaborative care observed in COINCIDE was the same as estimated from a meta-analysis of RCTs over a range of follow-up periods up to 24 months.[18] Comparison of the ICERs estimated from this model at 12, 24 and 36 months support the finding that collaborative care is better value over longer time horizons.[28] Economic evaluation of the medium-term (12 month) effects of collaborative care in the English healthcare system reported from CADET was similar to the 12-month results from our model.[26] The QALYs gained from collaborative care over 12 months (CADET 0.02; COINCIDE 0.03) and probability of cost-effectiveness at a WTPT of £20 000 (CADET 0.58; COINCIDE 0.53) were comparable. The estimated cost of delivering collaborative care (CADET £273; COINCIDE £317) and net cost of health service resources used were higher in COINCIDE (CADET £271; COINCIDE £560). This

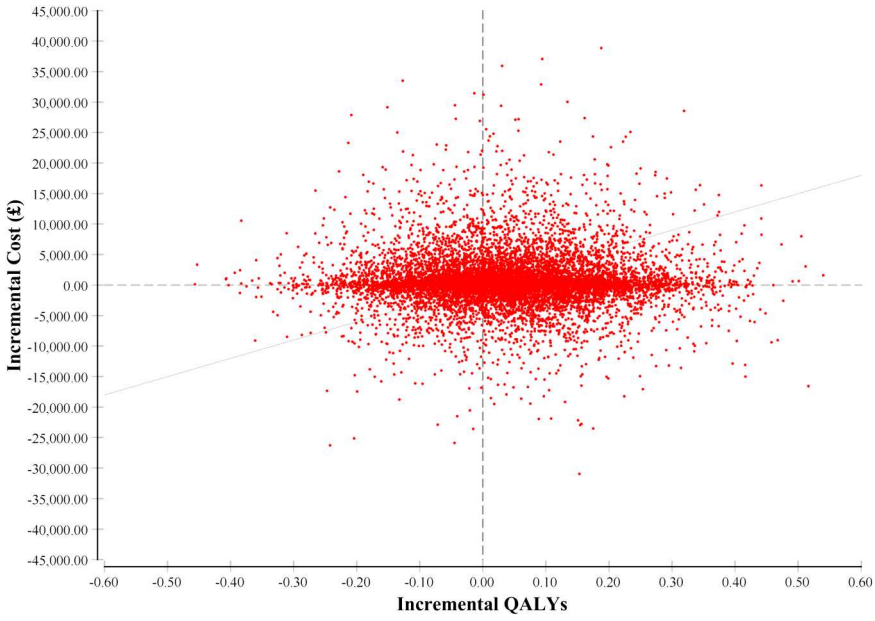

Figure 2 Incremental cost-effectiveness, collaborative care versus usual care. QALY, quality-adjusted life year.

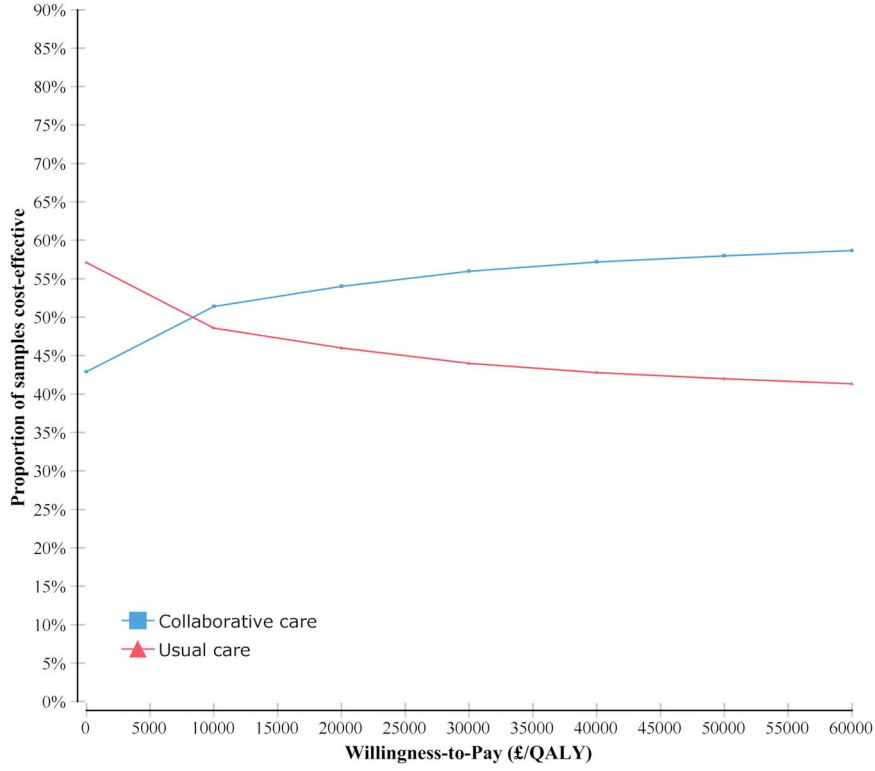

Figure 3 Cost-effectiveness acceptability curve. QALY, quality-adjusted life year.

suggests that for COINCIDE participants, collaborative care was associated with an impact on health service usage. This may result from improved self-care/management of physical health conditions.[20 27] This also reflects the specific impact of implementing collaborative care in patients with complex needs arising from multimorbidity and highlights the importance of examining this group as a special case. The mean QALY gain from collaborative care over 18–24 months reported in a systematic review[24] was the same as when it was assumed that the benefit of collaborative care observed during COINCIDE waned by 10% every 4 months. Even when it was assumed that the beneficial effect of collaborative care *increased* by 25% every 4 months, the estimated QALY gain over 24 months (0.21) did not reach the level estimated by a seemingly comparable US study (0.34).[25] This exemplifies the difficulty of generalising between studies and the need for health service-specific research.

Strengths and limitations

The parameters used in the decision model were derived from within-trial data and so are subject to the

same strengths and limitations as the trial.[19] COINCIDE was a large pragmatic trial (integrated within routine NHS settings) with good retention rates. A range of recruitment (eg, from diverse geographical/sociodemographic areas), randomisation (eg, cluster randomisation of practices) and analytic (eg, multiple imputation; adjusting for baseline characteristics) techniques were used to minimise bias and confounding and so ensure that the results of the economic evaluation are also likely to be robust and representative of routine practice.

Data regarding the usage of healthcare during the study period were self-reported by participants, collected via questionnaire at follow-up assessment. Participants may not be able to accurately recall each time they used a healthcare service, or may be unclear which category different services come under. These issues may affect people who use a large amount of healthcare services more. Verification against medical records may increase the reliability of these data; however, access to medical records was not agreed for COINCIDE participants.

There were 210 (54%) participants with complete EQ-5D (utility), healthcare usage (cost) and baseline covariate data. Multiple imputation of missing data for all COINCIDE participants reduced the potential for bias associated with missing data. However, the robustness of any imputation method declines as the level of missing data increases, reducing the validity and reliability of the analyses. For example, the high level of missing data and inconsistency of reporting for informal care received (from friends and family) meant that it was not possible to reliably impute data. The estimated cost-effectiveness may have been sensitive to the inclusion of informal care costs, but it is not possible to know the magnitude or direction of any effect. Findings reported here about the cost-effectiveness of collaborative care over 24 months (used to denote long-term follow-up in comparable trials of collaborative care[18]) were estimated from an extrapolation of short-term (4-month) trial data. The physical health conditions experienced by the cohort are long term and depression can also be a chronic, recurrent condition. The cost-effectiveness of collaborative care over 36 months (very long term) was explored in sensitivity analyses, but in this population, longer horizons (eg, 5–10 years) may also be important. There is already uncertainty around the ICERs estimated for 24 months. Extending the time horizon for this model would stretch the evidence from the trial too far (limiting robustness and increasing uncertainty). The economic model presented here demonstrated good external validity; results are supported by findings from other trials/reviews and the ICER changed as expected in response to the different one-way sensitivity analyses. Furthermore, the conclusion regarding cost-effectiveness and the probability that collaborative care is cost-effective did not vary greatly across sensitivity or subgroup analyses. This indicates that the model is robust. However, the probability of cost-effectiveness was conservative, even for an ICER of <£4000/QALY. This is due to differing levels of uncertainty around the estimates of costs and QALYs which can be seen by comparing the width of 95% CIs around the means (table 2 and see online supplementary table S3).

In a US study, collaborative care was associated with better self-management of diabetes and/or CHD.[20] There may be an important long-term impact of improved self-management on mortality (or other long-term health outcomes), especially among patients with multimorbidities. It was not possible to ascertain the long-term effect of collaborative care on morbidity and mortality for COINCIDE participants and so this was not explored further here.

CONCLUSION

These findings contribute to the evidence base in support of the commissioning of collaborative care for patients with depression in England. For the first time, it has been demonstrated that collaborative care may also be cost-effective in the English health service for patient groups with depression in conjunction with long-term physical health conditions, and over a long-term time horizon. However, the long-term findings were extrapolated from 4-month trial data and so associated with some uncertainty. Collection of long-term and very long-term clinical and cost-effectiveness data from a pragmatic RCT of collaborative care for patients with multimorbidities, which can be included in an updated meta-analysis, is needed to address this uncertainty.

Author affiliations
[1]Manchester Centre for Health Economics, University of Manchester, Manchester, UK
[2]Mental Health and Addiction Research Group, University of York, York, UK
[3]Centre for Primary Care, University of Manchester, Manchester, UK
[4]The School of Nursing, Midwifery and Social Work, University of Manchester, Manchester, UK
[5]Primary Care & Health Sciences, University of Keele, Staffordshire, UK
[6]NHS Health Education North West, Manchester, UK
[7]Mental Health Research Group, University of Exeter, Exeter, UK

Twitter Follow Peter Coventry at @peteyc73, Peter Bower at @Bowercpcman, Elizabeth Camacho @e_camacho_UoM and Linda Davies @lmdHE1

Contributors PC, KL, CD, PB, CC-G, CB, and LG were responsible for drafting and revising the original trial protocol. PC was the chief investigator and had overall responsibility for management of the trial. KL, CC-G, LG and CB delivered the training to practice nurses, psychological well-being practitioners and clinical supervisors. EMC and DN wrote the economic analysis plan and cleaned and analysed the data under supervision from LMD. EMC wrote the first draft of the report and revised subsequent drafts. All authors contributed to and approved the final report.

Funding This trial was funded by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care for Greater Manchester (CLAHRC-GM).

Disclaimer The views expressed in this article are those of the authors and not necessarily those of the NIHR, NHS, or the Department of Health.

Competing interests All authors had financial support from NIHR for the submitted work. LG had other support from Six Degrees—social enterprise that provides step 2 IAPT services.

Ethics approval The study was approved by the National Research Ethics Service Committee North West-Preston (NRES/11/NW/0742); research governance approvals were granted by participating primary care trusts and informed consent was given by all patients.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

REFERENCES

1. McManus S, Meltzer H, Brugha TS, *et al*. Adult psychiatric morbidity in England, 2007: results of a household survey. London: England NHS Information Centre for Health and Social Care, 2009.
2. Goldney RD, Phillips PJ, Fisher LJ, *et al*. Diabetes, depression, and quality of life: a population study. *Diabetes Care* 2004;27:1066–70.
3. Anderson RJ, Freedland KE, Clouse RE, *et al*. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care* 2001;24:1069–78.
4. Naylor C, Parsonage M, McDaid D, *et al*. *Long-term conditions and mental health: the cost of co-morbidities*. King's Fund and Centre for Mental Health, 2012.
5. Carney RM, Freedland KE, Sheps DS. Depression is a risk factor for mortality in coronary heart disease. *Psychosom Med* 2004;66:799–801.
6. Bhattarai N, Charlton J, Rudisill C, *et al*. Prevalence of depression and utilization of health care in single and multiple morbidity: a population-based cohort study. *Psychol Med* 2013;43:1423–31.
7. Von Korff M, Katon W, Lin EH, *et al*. Potentially modifiable factors associated with disability among people with diabetes. *Psychosom Med* 2005;67:233–40.
8. Piette JD, Heisler M, Wagner TH. Cost-related medication underuse among chronically Ill adults: the treatments people forgo, how often, and who is at risk. *Am J Public Health* 2004;94:1782–7.
9. Coventry PA, Hays R, Dickens C, *et al*. Talking about depression: a qualitative study of barriers to managing depression in people with long term conditions in primary care. *BMC Fam Pract* 2011;12:10.
10. Ridd M, Shaw A, Salisbury C. 'Two sides of the coin'—the value of personal continuity to GPs: a qualitative interview study. *Fam Pract* 2006;23:461–8.
11. Chew-Graham CA. Patients with chronic physical illness and co-existing psychological morbidity: GPs' views on their role in detection and management. *Int J Psychiatry Clin Pract* 2002;8:35–9.
12. Chew-Graham CA, Hunter C, Langer S, *et al*. How QOF is shaping primary care review consultations: a longitudinal qualitative study. *BMC Fam Pract* 2013;14:103.
13. Department of Health. *No health without mental health: a cross-government mental health outcomes strategy for people of all ages*. London: Stationery Office, 2011.
14. World Health Organisation. Mental health: facing the challenges, building solutions. *Report from the WHO European Ministerial Conference;* World Health Organisation, 2005.
15. Richards DA, Hill JJ, Gask L, *et al*. Clinical effectiveness of collaborative care for depression in UK primary care (CADET): cluster randomised controlled trial. *BMJ* 2013;347:f4913.
16. Coventry PA, Lovell K, Dickens C, *et al*. Collaborative Interventions for Circulation and Depression (COINCIDE): study protocol for a cluster randomized controlled trial of collaborative care for depression in people with diabetes and/or coronary heart disease. *Trials* 2012;13:139.
17. Coventry PA, Lovell K, Dickens C, *et al*. Update on the collaborative interventions for circulation and depression (COINCIDE) trial: changes to planned methodology of a cluster randomized controlled trial of collaborative care for depression in people with diabetes and/or coronary heart disease. *Trials* 2013;14:136.
18. Archer J, Bower P, Gilbody S, *et al*. Collaborative care for depression and anxiety problems. *Cochrane Database Syst Rev* 2012;10:CD006525.
19. Coventry P, Lovell K, Dickens C, *et al*. Integrated primary care for patients with mental and physical multimorbidity: cluster randomised controlled trial of collaborative care for patients with depression comorbid with diabetes or cardiovascular disease. *BMJ* 2015;350:h638.
20. Katon WJ, Lin EH, Von Korff M, *et al*. Collaborative care for patients with depression and chronic illnesses. *N Engl J Med* 2010;363:2611–20.
21. Katon WJ, Schoenbaum M, Fan MY, *et al*. Cost-effectiveness of improving primary care treatment of late-life depression. *Arch Gen Psychiatry* 2005;62:1313–20.
22. Lin EH, Katon W, Von Korff M, *et al*. Effect of improving depression care on pain and functional outcomes among older adults with arthritis: a randomized controlled trial. *JAMA* 2003;290:2428–9.
23. Katon WJ, Von Korff M, Lin EH, *et al*. The pathways study: a randomized trial of collaborative care in patients with diabetes and depression. *Arch Gen Psychiatry* 2004;61:1042–9.
24. Jeeva F, Dickens C, Coventry P, *et al*. Is treatment of depression cost-effective in people with diabetes? A systematic review of the economic evidence. *Int J Technol Assess Health Care* 2013;29:384–91.
25. Katon W, Russo J, Lin EH, *et al*. Cost-effectiveness of a multicondition collaborative care intervention: a randomized controlled trial. *Arch Gen Psychiatry* 2012;69:506–14.
26. Green C, Richards DA, Hill JJ, *et al*. Cost-effectiveness of collaborative care for depression in UK primary care: economic evaluation of a randomised controlled trial (CADET). *PLoS ONE* 2014;9:e104225.
27. Lin EH, Katon W, Von Korff M, *et al*. Relationship of depression and diabetes self-care, medication adherence, and preventive care. *Diabetes Care* 2004;27:2154–60.
28. Walker S, Walker J, Richardson G, *et al*. Cost-effectiveness of combining systematic identification and treatment of co-morbid major depression for people with chronic diseases: the example of cancer. *Psychol Med* 2014;44:1451–60.
29. Drummond MF, Sculpher MJ, Torrance GW, *et al*. *Methods for the economic evaluation of health care programmes*. New York: Oxford University Press, 2005.
30. BMA and NHS Employers Association. *Quality and outcomes framework guidance for GMS contract 2011/2012*. London: Delivering Investment in General Practice, 2011.
31. Kroenke K, Spitzer RL, Williams JB. The Phq-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606–13.
32. National Collaborating Centre for Mental Health, National Institute for Clinical Excellence. *Depression in adults with a chronic physical health problem: recognition and management—CG91*. National Institute for Clinical Excellence, 2009.
33. Derogatis LR, Cleary PA. Confirmation of the dimensional structure of the SCL-90: a study in construct validation. *J Clin Psychol* 1977;33:981–9.
34. Brooks R, Group E. EuroQol: the current state of play. *Health Policy* 1996;37:53–72.
35. Herdman M, Gudex C, Lloyd A, *et al*. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* 2011;20:1727–36.
36. National Institute for Clinical Excellence. *Guide to the methods of technology appraisal*. National Institute for Clinical Excellence, 2013.
37. Peasgood T, Brazier J, Papaioannou D. *A systematic review of the validity and responsiveness of EQ-5D and SF-6D for depression and anxiety*. HEDS Discussion paper 12/15. 2012.
38. Curtis L. *The unit costs of health and social care 2012*. Kent: Personal Social Services Research Unit, 2013.
39. Department of Health. *National schedule of reference costs 2011–2012*. Department of Health, 2013.
40. Joint Formulary Committee, Royal Pharmaceutical Society of Great Britain. *British national formulary*. 64th edn. Pharmaceutical Press, 2012.
41. Bernstein IH, Wendt B, Nasr SJ, *et al*. Screening for major depression in private practice. *J Psychiatr Pract* 2009;15:87.
42. Briggs MA, Sculpher M. An introduction to Markov modelling for economic evaluation. *Pharmacoeconomics* 1998;13:397–409.
43. Briggs AH, O'Brien BJ. The death of cost-minimization analysis? *Health Econ* 2001;10:179–84.
44. Fenwick E, Claxton K, Sculpher M. Representing uncertainty: the role of cost-effectiveness acceptability curves. *Health Econ* 2001;10:779–87.
45. Hoch JS, Briggs AH, Willan AR. Something old, something new, something borrowed, something blue: a framework for the marriage of health econometrics and cost-effectiveness analysis. *Health Econ* 2002;11:415–30.
46. Pedram Sendi P, Briggs AH. Affordability and cost-effectiveness: decision-making on the cost-effectiveness plane. *Health Econ* 2001;10:675–80.

BMJ Open

Long-term cost-effectiveness of collaborative care (vs usual care) for people with depression and comorbid diabetes or cardiovascular disease: a Markov model informed by the COINCIDE randomised controlled trial

Elizabeth M Camacho, Dionysios Ntais, Peter Coventry, Peter Bower, Karina Lovell, Carolyn Chew-Graham, Clare Baguley, Linda Gask, Chris Dickens and Linda M Davies

BMJ Open 2016 6:
doi: 10.1136/bmjopen-2016-012514